

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE." Entry of these amendments is respectfully requested.

The Office Action notes that a Sequence Listing is required. In response to this requirement, Applicants submits concurrently herewith a paper and computer readable copy of the Sequence Listing.

#### Rejection Under 35 U.S.C. § 112, Second paragraph

Claims 11-13 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as their invention. Specifically, the Office Action asserts that the phrase "said sugar phosphates" in claims 11 and 12 lack antecedent basis. Applicants have amended herewith claim 11 to provide the proper antecedent basis. As a result, claim 12, which depends on claim 11, is now in proper form. Claim 13, which depends from claim 12, was also rejected. In view of the amendment to claim 11, claims 11-13 are now in proper form for allowance.

The Office Action further rejected claim 14, asserting that the term "the length" is lacking proper antecedent basis. Claim 14 is amended herewith to correct the improper antecedent basis. Support for these amendments may be found in the originally filed claims. Withdrawal of the rejection is respectfully requested.

#### Rejection Under 35 U.S.C. § 102(e)

Claims 1-6, 8-14, 16-18 and 25 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lizardi (U.S. 5,854,033), Oku et al. (EP 0 698 792 A1), or Fields et al. (WO 94/26932). Applicants respectfully traverse the rejections.

#### *Lizardi (U.S. 5,854,033)*

The Office Action asserts that Lizardi teaches a DNA tag linked to an antibody, and that this anticipates the claims of the present invention. A proper rejection for anticipation

under 35 U.S.C. § 102(e) requires that the “claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Applicants respectfully assert that Lizardi does not anticipate the claimed invention because Lizardi does not teach each and every element of the claims.

Lizardi teaches a DNA-labeled reporter antibody. The DNA tag used by Lizardi is shown as 45 bp (see Fig. 9), but otherwise is not described in detail. In fact, the DNA tags described in Example 5 (Column 40) are only described as “arbitrary” and 50 nucleotides long. As such, Lizardi fails to teach or suggest a DNA tag that is a block copolymer, much less a molecular bar code that includes a block copolymer tag.

As amended, the claims in the instant application are directed to a molecular bar code that includes a block copolymer as the tag.

As demonstrated above, Lizardi does not teach that the DNA tag is a block copolymer of known composition, comprised of a plurality of blocks, as is described in amended claim 1, or independent claims 8 and 16 of the present invention. Therefore, Lizardi does not anticipate the claimed invention and withdrawal of the rejection is respectfully requested.

*Oku et al. (EP 0 698 792 A1)*

Applicants note that Oku et al. is a European patent, and will assume that the Office meant to reject the claims under 35 U.S.C. § 102(b).

The Office Action asserts that Oku et al. teach an oligonucleotide tag linked to an antibody.

A proper rejection for anticipation under 35 U.S.C. § 102(b) requires that the “claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Id.* Applicants respectfully assert that Oku et al. do not anticipate the claimed invention because Oku et al. do not teach every element of the claims.

Oku et al. teach a 20 bp synthesized oligonucleotide ligated to the antibody must be complementary to the oligonucleotide on the solid support (see Fig. 5, p. 4, lines 15-32, p. 7, lines 28-30, and p. 8, lines 23-26). The following five oligonucleotides were disclosed:



Amino group-GAA TTC CCG GGG ATC CGT CG, Amino group-GCC AAG CTT GGC TGC AGG TC, Amino group-AAG CTT GCA TGC CTG CAG GT, Amino group-GGC GAC TGT CGA ACC GGA AA, and Amino group-CCA CCC CTA CTC CTA ATC CC. As such, Oku does not teach or suggest a tag that is a block copolymer.

In contrast, the claims in the instant application are directed to a molecular bar code that includes a block copolymer as the readable tag.

Because Oku et al. do not teach an oligonucleotide tag which is a block copolymer comprised of a plurality of different blocks, as is described in amended claim 1, or independent claims 8 and 16 of the present invention, Oku et al. do not anticipate the claimed invention. Withdrawal of the rejection is respectfully requested.

*Fields et al. (WO 94/26932)*

Applicants note that Fields et al. is a WIPO application and will assume that the Office meant to reject the claims under 35 U.S.C. § 102(b).

The Office Action asserts that Fields et al. teach an oligonucleotide tag linked to an antibody, and that this anticipates the claimed invention.

A proper rejection for anticipation under 35 U.S.C. § 102(b) requires that the “claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Id.* Fields et al. do not anticipate the claimed invention because Fields et al. do not teach every element of the claims.

Fields et al. teach only an oligonucleotide-linked ligand with a known sequence. The oligonucleotide is synthetic, preferably short, with a weak secondary structure (see p. 9, line 23 to p. 10, line 12 and p. 13, lines 17-20). An example of an oligonucleotide tag is shown on p. 10, line 36: 5'-cct ccc cta tct tct cct ccc caa caa aaa aaa aaa aaa a-3'. The only requirement appears to be that the oligonucleotide can be successfully linked with the ligand of interest. As such, Fields et al fail to teach or suggest that the tag could be a block copolymer.

As explained above, the claims of the instant application are directed to a molecular bar code that includes a tag that is made up of a plurality of polymeric blocks, i.e., that includes a block copolymer.

Because Fields et al. do not teach or suggest that the oligonucleotide tag is a block copolymer comprised of a plurality of blocks, as is described in amended claim 1, or independent claims 8 and 16 of the present invention, Fields et al. do not anticipate the claimed invention. Withdrawal of this rejection is therefore respectfully requested.

The invention of the instant application is not anticipated by any of the cited references. None of the three cited references disclose each and every element of the claimed invention, that is, the block copolymers comprised of a plurality of blocks. Therefore, the rejection under 35 U.S.C. § 102(e) or 102(b) is not proper, and should be withdrawn.

#### **Rejections Under 35 U.S.C. § 103(a)**

Claims 26-29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over either Lizardi (US 5,854,033), Oku et al. (EP 0 698 792 A1), or Fields et al. (WO 94/26932). Applicants respectfully traverse the rejections.

The Office Action asserts that although Lizardi, Oku et al., or Fields et al. do not disclose different nucleic acid tags, it would have been obvious to use different nucleic acid tags, each for detecting a different analyte, in order to simultaneously detect multiple analytes in a kit.

A proper rejection for obviousness under 35 U.S.C. § 103(a) requires that at the time the invention was made, the invention as a whole would have been obvious to one of skill in the art in view of the prior art. The M.P.E.P. provides clear guidance on the requirements of a *prima facie* case of obviousness:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2142.



Claims 26-29 of the instant invention are directed towards kits that include a plurality of different molecular bar codes, where the bar codes include block copolymer tags.

As demonstrated above, Lizardi, Oku and Fields are all deficient in that they fail to teach or suggest a molecule that includes a block copolymer as a tag, much less the claimed molecular bar codes.

As such, Claims 26-29 are not obvious under 35 U.S.C. § 103(a) over either Lizardi (US 5,854,033), Oku et al. (EP 0 698 792 A1), or Fields et al. (WO 94/26932) and this rejection may be withdrawn.

Claims 7, 15, and 19 were rejected under 35 U.S.C. § 103(a) as being unpatentable over either Lizardi (U.S. 5,854,033), Oku et al. (EP 0 698 792 A1), or Fields et al. (WO 94/26932), each in view of Rothschild et al. (U.S. 5,986,076). Applicants respectfully traverse the rejection.

The Office Action asserts that Rothschild et al. disclose photocleavable biotin conjugates for nucleic acid and proteins, and that in view of Lizardi, Oku et al., or Fields et al., it would have been obvious to use the photocleavable biotin to link the antibody and molecular bar code because the photocleavable biotin is easily and selectively cleaved with electromagnetic radiation.

As pointed out above, the primary references (Lizardi, Oku et al., and Fields et al.) are fundamentally deficient in failing to teach or suggest the block copolymer component of the claimed molecular bar codes. As the Rothschild reference is cited solely for its teaching of a photocleavable linker, it fails to make up this fundamental deficiency in the primary references.

Accordingly, Claims 7, 15, and 19 are not obvious under 35 U.S.C. § 103(a) over either Lizardi (U.S. 5,854,033), Oku et al. (EP 0 698 792 A1), or Fields et al. (WO 94/26932), each in view of Rothschild et al. (U.S. 5,986,076) and this rejection may be withdrawn.

### CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is respectfully requested. If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.



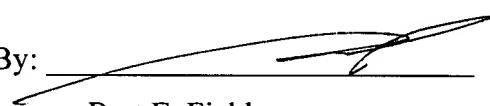
The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL118.

Respectfully submitted,

BOZICEVIC, FIELD & FRANCIS LLP

Date: 8.10.01

By:

  
Bret E. Field  
Registration No. 37,620

BOZICEVIC, FIELD & FRANCIS LLP  
200 Middlefield Road, Suite 200  
Menlo Park, CA 94025  
Telephone: (650) 327-3400  
Facsimile: (650) 327-3231

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Specification**

Page 24, lines 10 and 11

--5nitroindole(20)/Spacer9/dT(1)/Spacer9/dT(17)TCTAGAGCGCTTGCGCTCTAGA/  
Spacer 18/GTGTCCAATGACAACGATGTTGATGTGAGTCTTCCTT (SEQ ID  
NO:02)--

**In the Claims**

1. (Amended) A targeted molecular bar code comprising:

(a) a molecular bar code that is a block copolymer of a plurality of blocks selected from two or more different blocks, wherein said molecular bar code is a charged polymer capable of generating a reproducible signal upon passage through a nanopore; and

(b) a member of a specific binding pair, wherein said specific binding pair member is joined directly or through a linking group to said molecular bar code.

Cancel claim 4.

5. (Amended) The targeted molecular bar code according to Claim 1 4, wherein said block copolymer comprises three different blocks.

11. (Amended) The targeted molecular bar code according to Claim 8-10, wherein said sugar phosphates are selected from the group consisting of ribose phosphates and deoxyribose phosphates.

14. (Amended) The targeted molecular bar code according to Claim 8, wherein the length of each block of said block copolymer ranges has a length ranging from 15 to 25 nm.

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